

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE  
 in its capacity as elected Office

Date of mailing (day/month/year)

07 December 2000 (07.12.00)

International application No.

PCT/US00/06808

Applicant's or agent's file reference

655000038PPA

International filing date (day/month/year)

16 March 2000 (16.03.00)

Priority date (day/month/year)

23 March 1999 (23.03.99)

Applicant

FROST, John, W. et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

20 October 2000 (20.10.00)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Charlotte ENGER

Telephone No.: (41-22) 338.83.38

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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/06808

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : C12P 7/00, 39/00

US CL : 435/132, 42

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/132, 42

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

STN, search terms: 642-96-6 (Registry No. for 1,2,3,4-tetrahydroxybenzene), inositol, inosose, dehydrogenase, synthase, metabolism, microorganism, yeast, review

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P --- Y, P	HANSEN et al. Synthesis of 1,2,3,4-Tetrahydroxybenzene from D-Glucose. Journal of the American Chemical Society. 21 April 1999, Vol. 121, pages 3799-3800, see entire document.	1-10, 12, 14-23, 30-31 ----- 11,13,24-29, 32-57
Y	YOSHIDA et al. Organization and Transcription of the <i>myo</i> -Inositol Operon, <i>iol</i> , of <i>Bacillus subtilis</i> . Journal of Bacteriology. July 1997, Vol. 179, No. 14, pages 4591-4598, see entire document.	11, 24-29, 32-33, 50-55
Y	DEAN-JOHNSON et al. Biosynthesis of Inositol in Yeast. The Journal of Biological Chemistry. 15 January 1989, Vol. 264, No. 2, pages 1274-1283, see entire document.	3-6, 15-18, 22-24, 29, 31, 33, 36-39, 48-50, 54-55

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* "A"	Special categories of cited documents: document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E"	earlier document published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

12 JUNE 2000

Date of mailing of the international search report

05 JUL 2000

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

KATHLEEN KERR

Telephone No. (703) 308-0198

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/06808

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WHITE et al. Inositol Metabolism in Yeasts. Advances in Microbial Physiology. London: Academic Press, 1991, Vol. 32, pages 1-51.	1-57

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/06808

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/06808

### BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1.

Group I, claims 1-33, drawn to methods for the production of 1,2,3,4-tetrahydroxybenzene.

Group II, claims 34-57, drawn to methods for the production of 1,2,3-trihydroxybenzene.

The inventions listed as Groups I and II do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of Group I is the methods for producing 1,2,3,4-tetrahydroxybenzene via myo-inositol and myo-2-inosose in recombinant microbes. This special technical feature does not relate to the same inventive concept as the methods for producing a distinct compound, namely 1,2,3-trihydroxybenzene, although some of the microbes used can be identical between the two inventive concepts.

Although the Examiner finds a lack of unity between the two Groups, the Examiner will examine both Groups in the search report because the search for each of the Groups is somewhat overlapping. Thus, the invention of the methods for producing 1,2,3,4-tetrahydroxybenzene and the invention of the methods for producing 1,2,3-trihydroxybenzene have been searched. The Examiner reserves the right to uphold this lack of unity in the Chapter 2 phase of this PCT case.

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 03 AUG 2001

Applicant's or agent's file reference 655000038PPA	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/06808	International filing date (day/month/year) 16 MARCH 2000	Priority date (day/month/year) 23 MARCH 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): C12P 7/00, 39/00 and US Cl.: 435/132, 42		
Applicant BOARD OF TRUSTEES OPERATING MICHIGAN STATE UNIVERSITY		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 20 OCTOBER 2000	Date of completion of this report 10 JULY 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer KATHLEEN KERR TERRY J. DEY PARALEGAL SPECIALIST TECHNOLOGY CENTER 1600
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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/06808

**I. Basis of the report**1. With regard to the **elements** of the international application: \*

- ☒ the international application as originally filed
- ☒ the description:  
pages 1-23, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the claims:  
pages 24-29, as originally filed  
pages NONE, as amended (together with any statement) under Article 19  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the drawings:  
pages 1-4, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the sequence listing part of the description:  
pages NONE, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.  
These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/fig NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

**IV. Lack of unity of invention**

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

Group I, claims 1-33, drawn to methods for the production of 1,2,3,4-tetrahydroxybenzene.

Group II, claims 34-57, drawn to methods for the production of 1,2,3-trihydroxybenzene.

The inventions listed as Groups I and II do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of Group I is the methods for producing 1,2,3,4-tetrahydroxybenzene via myo-inositol and myo-2-inosose in recombinant microbes. This special technical feature does not relate to the same inventive concept as the methods for producing a distinct compound, namely 1,2,3-trihydroxybenzene, although some of the microbes used can be identical between the two inventive concepts.

Although the Examiner finds a lack of unity between the two Groups, the Examiner will examine both Groups because the search for each of the Groups is somewhat overlapping. Thus, the invention of the methods for producing 1,2,3,4-tetrahydroxybenzene and the invention of the methods for producing 1,2,3-trihydroxybenzene have been searched.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos. .



## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/06808

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

## 1. statement

Novelty (N)	Claims <u>1-57</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>1-57</u>	YES
	Claims <u>NONE</u>	NO
Industrial Applicability (IA)	Claims <u>1-57</u>	YES
	Claims <u>NONE</u>	NO

## 2. citations and explanations (Rule 70.7)

Claims 1-57 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the instant methods for the production of 1,2,3,4-tetrahydroxybenzene or 1,2,3-trihydroxybenzene. While the prior art teaches the INO1 gene from *Saccharomyces cerevisiae*, the prior art does not teach or suggest the use of said gene in the methods of the instant claims. While the prior art teaches the iolG gene from *Bacillus subtilis*, the prior art does not teach or suggest the use of said gene in the methods of the instant claims. The prior art teaches acid catalyzed dehydration of myo-2-inosose renders 1,2,3,5-tetrahydroxybenzene and not 1,2,3,4-tetrahydroxybenzene as claimed by Applicants. Thus, Claims 1-57 are deemed novel and free of the prior art.

----- NEW CITATIONS -----  
NONE

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

Claim 13 is objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof. The term "1,2,3,-tetrahydroxybenzene" is a typographical error; the correct term is ---1,2,3,4-tetrahydroxybenzene---

Claims 21, 22, 25, 30, 31, 47, 48, and 51 are objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof. The instant claims use the phrase "encoding for"; the correct term in the art is ---encoding--- without using the preposition "for".

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The description is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 5 because it fails to contain an adequate enablement and written description of Claims 1, 20, 34, and 46. The description is inadequate for the following reasons.

The instant description describes methods of making 1,2,3,4-tetrahydroxybenzene and its derivative, 1,2,3-trihydroxybenzene, using microbes to produce myo-inosose. Said microbes must contain a gene encoding a myo-inositol-1-phosphate synthase and an inositol dehydrogenase, as described in Figure 2 of the instant specification, to convert the starting material, a carbon source, into myo-inosose which is then subjected to catalytic dehydration, optionally coupled to a reduction step. The instant description does not describe or enable the instant methods using microbes which do not contain genes encoding myo-inositol-1-phosphate synthase and inositol dehydrogenase. Clearly, the instant claims intend to claim such breadth as understood by the dependent claims 2, 7, 21, 35, 40, and 47, which otherwise would not further limit the parent claims.

Claims 1, 20, 34, and 46 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not adequately described in writing, as required under PCT Rule 5.1(a)(iii), for the reasons set forth in the immediately preceding paragraph. Claims 1, 20, 34, and 46 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph.

Claims 1-3, 7, 10, 11, 14, 20, 21, 22, 25, 26, 30, 34, 35, 40, 46-48, 51, and 52 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s):

Claims 1, 14, 20, 30, 34, and 46 are indefinite because said claims claim methods of producing derivatives of 1,2,3,4-tetrahydroxybenzene while the method only produces 1,2,3,4-tetrahydroxybenzene, not its derivatives as well. The term "and derivatives thereof" must be deleted or additional method steps must be added to the instant claims.

Claims 2, 10, 14, 21, 30, 35, and 47 are indefinite because of the term "comprises the gene[s]"; "comprises" is not the appropriate term of the art since expression of the genes is required, as described in the instant description. (Continued on Supplemental Sheet.)

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**VIII. CERTAIN OBSERVATIONS ON THE APPLICATION (Continued):**

Thus, in the instant claims "comprising" must be replaced with ---expressing---.

Claims 2, 10, 14, 21, 30, 35, and 47 are indefinite because they refer to a generic enzyme names, "myo-inositol-1-phosphate synthase" or "inositol dehydrogenase", with the article "the" indicating a single gene. In the instant claims, "the gene" must be replaced with ---a gene---.

Claims 3, 11, 22, 26, 48, and 52 are indefinite because they refer to specific gene names, "S. cerevisiae INO1 gene" or "Bacillus subtilis iolG gene", with the article "a" indicating multiple genes. In the instant claims, "a gene" must be replaced with ---the gene---.

Claims 7, 14, and 40 are indefinite for the improper use of the term "activity". In the art, the enzyme name indicates activity so the use of this term is redundant. In the instant claims, the term "activity" must be deleted.

Claims 25 and 51 are indefinite for the use of the term "an iolG gene". The article "an" and the further dependent claims limiting the instant gene to the Bacillus subtilis gene indicates that more than one iolG gene is indicated in the instant claims. However, neither the description nor the art indicate an iolG gene in an organism other than Bacillus subtilis. Appropriate information must be set forth or the instant claims must be cancelled.